REMARKS

The Examiner previously issued a Restriction Requirement, and in response to that Restriction Requirement, Applicants elected the claims of Group III. The claims have been amended herein to claim the diazabicyclononanes of elected Group III. Claims 5, 16, 26, and 37, which would have included diazabicycloheptanes, have accordingly been cancelled. Claims 11 and 32, which also listed specific diazabicycloheptanes, have also been cancelled. The claims have also been amended to further define the list of non-hydrogen substituents, as requested by the Examiner. The subject matter that has been removed by this amendment is done so without prejudice and Applicants reserve the right to pursue broader claims in a related application. Finally, the structure has been amended so that the R group formerly attached to N has been limited to H. It is believed that the claims as amended overcome all of the objections and rejections raised by the October 10, 2002 Office Action.

Election/Restriction Requirement

The Examiner acknowledged Applicants' election of Group III, as well as Applicants' election of the species 3-(5-phenoxy-3-pyridyl)-3,7-diazabicyclo[3.3.1]nonane. The Examiner requested that Applicants amend the claims to limit them solely to the [3.3.1]nonane structure. Applicants have amended the claims such that the values of u, v, w, and x, are selected such that the ring is a diazabicyclononane. This is consistent with Applicants' election of Group III. Upon indication of an allowable Species, it is understood that the Examiner will then broaden the search to include the remainder of the elected Group, and the elected Group reads more broadly than just the [3.3.1]nonane structure. Applicants believe the amendment made is consistent with the election requirement.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1-10, 12-31 and 33-42 have been rejected under 35 U.S.C. § 112, first paragraph as non-enabled. In particular, the claims formerly defined "D" and "Z" as non-hydrogen substituents. The claims have been amended to include the specific functional groups listed in the specification, thus obviating the rejection.

Further, the Office Action states that the specification fails to teach the preparation of compounds with a [3.3.1]nonane core. This is not the case. The specification teaches (page 17, first paragraph) how to prepare compounds with a [3.3.1]nonane ring system, and also teaches (page 16, first full paragraph) how to prepare compounds with a [3.2.2]nonane ring system. A number of representative compounds (24 individual compounds) with a [3.3.1] or [3.2.2] nonane core are shown, for example, on pages 10-11. Further, the manner in which the compounds of the invention can be prepared, generally, is described in the specification on pages 11-17. The Office Action provides no legitimate basis to conclude that the compounds cannot be prepared using the teaching provided by the specification. Accordingly, Applicants respectfully request that this ground of rejection be withdrawn.

The Office Action also stated that in the absence of testing data, there is no reasonable assurance that the compounds have the desired activity. There is no requirement for actual working examples. Although numerous working examples are provided in the specification, it is true that no working examples relate to the specific group that was elected. However, there is sufficient guidance regarding the synthesis of these compounds and how they can be tested for activity at nicotinic receptors that those of skill in the art would not require undue experimentation to make and test the compounds as presently claimed. Applicants' specification teaches that these compounds are active at nicotinic receptors, and the Office Action provides no credible scientific evidence that they are not. Accordingly, this ground of rejection should be withdrawn.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1, 6, 12, 22 and 33 have been rejected under 35 U.S.C. § 112, first paragraph as non-enabled. The claims formerly defined "D" and "Z" as non-hydrogen substituents, and as substituents having a sigma m value between about -0.3 and about 0.75. The claims have been amended to include the specific functional groups listed in the specification, thus obviating the rejection.

Further, the Office Action stated that the terms "heterocyclyl," "substituted," "substituent species," and "aromatic group-containing species" are unclear. The term "heterocyclyl" is

defined in the specification as "saturated or unsaturated cyclic radicals containing one or more heteroatoms (e.g., O, N, S) as part of the ring structure and having two to seven carbon atoms in the ring; "substituted heterocyclyl" refers to heterocyclyl radicals further bearing one or more substituent species as defined above" (page 7, lines 15-18). Those of skill in the art, particularly after reviewing the instant specification, understand what is meant by this term. Representative heterocyclic groups are listed in the specification, providing additional guidance to those of skill in the art.

The terms "substituted" and "substituent species" have been clarified by virtue of the additional definition of suitable substituents. The term "aromatic group-containing species" has been clarified by amending the claims to specifically list those aromatic group-containing species specifically listed in the specification.

It is believed that these amendments overcome the rejections. Accordingly, Applicants respectfully request that the rejections be withdrawn in view of the amended claims.

Rejections Under 35 U.S.C. § 103 (a)

Claims 1-10, 12-31 and 33-42 have been rejected under 35 U.S.C. § 103 (a) as obvious in view of PCT WO 97/40049 to Czollner et al. Czollner teaches diazabicyclic compounds which require the presence of an aromatic group or a methyl group at position R22, which corresponds to an attachment to the nitrogen in the presently claimed diazabicyclic compounds that is not attached to Cy. The claims have been amended to define the group attached to this ring nitrogen as H, rather than R, and this amendment is believed to obviate the rejection. Czollner specifically requires that the substitution at R22 is aryl, substituted aryl, methyl or substituted methyl. To clarify this, Applicants provide a translation of the definition of R_{22} (from page 8, lines 1-9 of PCT WO 97/40049 to Czollner et al.):

wherein R_{22} is

An unsubstituted or one substituted by one or more of F, Cl, Br, I, NO_2, NH_2, OH, alkyl, alkyloxy, CN, NC, or CF_3, CHO, COOH, COOalkyl, SO_3H, SH, S-alkyl groups equally or unequally substituted by two unsubstituted **(hetero) aryl residues** or

a **methyl group** substituted by two unsubstituted or substituted by one or more of F, Cl, Br, I, NO_2, NH_2, OH, alkyl, alkyloxy, CN, NC, or CF_3, CHO, COOH, COOalkyl, SO_3H, SH, S-alkyl groups or differently substituted phenyl group(s). *(emphasis added)*

Despite a wide variety of possible substituents that purportedly provide similar activity, Czollner provides absolutely no motivation to modify R22 to be any substituents other than the specifically listed aryl or methyl groups, let alone H as instantly claimed. Accordingly, Applicants respectfully request that the obviousness rejection be withdrawn in view of the amended claims.

Conclusion

Applicant respectfully urges that upon entry of the above amendment, claims 1-4, 6-10, 12-25, 27-31, 33-36, and 38-42 are in condition for allowance. However, if Examiner believes that any issues remain unresolved, Applicant respectfully requests that Examiner contact the undersigned attorney.

Respectfully submitted,

Date: March 10, 2003

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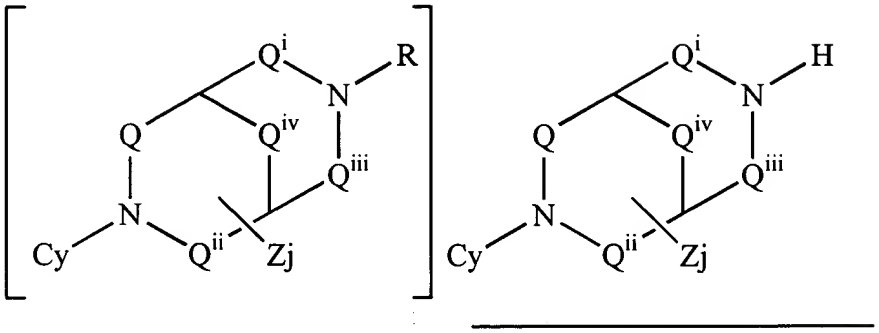
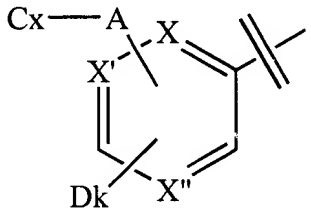
APPENDIX

Amended Claims

1. (Amended) A compound of the formula:



wherein Q is $(CH_2)_u$, Q^i is $(CH_2)_v$, Q^{ii} is $(CH_2)_w$, Q^{iii} is $(CH_2)_x$, and Q^{iv} is $(CH_2)_y$, where u, v, w and x are individually 0, 1, 2, 3 or 4 and y is 1 or 2; wherein u, v, w and x are selected such that the ring is a diazabicyclononane; Z is a [non-hydrogen] substituent species [characterized as having a sigma m value between –0.3 and about 0.75] G; j is from 0 to 10; R is hydrogen or [lower] C_{1-8} alkyl; and Cy is



where each of X, X' and X" are individually nitrogen, nitrogen bonded to oxygen or carbon bonded to a substituent species [characterized as having a sigma m value between –0.3 and about 0.75] G; A is O or C=O; D is a [non-hydrogen] substituent species [characterized as having a sigma m value between –0.3 and about 0.75] G; k is 0, 1 or 2; and Cx is selected from a group consisting of aryl, substituted aryl, heteroaryl, substituted heteroaryl, non-aromatic

heterocyclyl, substituted non- aromatic heterocyclyl, non-aromatic heterocyclylalkyl and substituted non-aromatic heterocyclylalkyl,

wherein G is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, non-aromatic heterocyclyl, substituted non-aromatic heterocyclyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, alkylaryl, substituted alkylaryl, arylalkyl, substituted arylalkyl, -F, -Cl, -Br, -I, -OR', -NR'R $-CF_3$, -CN, $-N_3$, $-NO_2$, $-C_2$ R', -SR', -SOR', $-SO_2$ CH_3, $-SO_2$ NR'R -C(=O)NR'R", -NR'C(=O)R -NR'SO_2 R -C(=O)R', -C(=O)OR', $-(CH_2)$qOR', -OC(=O)R', $-(CR'R)_0OCH_2C_2$ R', -(CR'R)qC(=O)R', $-O(CR'R)_qC(=O)R'$, $-C_2(CR'R')_qOR'$, $-(CR'R)_qNR'R$ -OC(=O)NR'R and -NR'C(=O)OR' where R' and R are individually hydrogen, C_{1-8} alkyl, an aromatic group-containing species or a substituted aromatic group-containing species, wherein the substituent is G and the aromatic group containing species is phenyl, biphenyl, naphthyl, pyridinyl, pyrimidinyl, quinolinyl, or indolyl, and

q is an integer from 1 to 6.

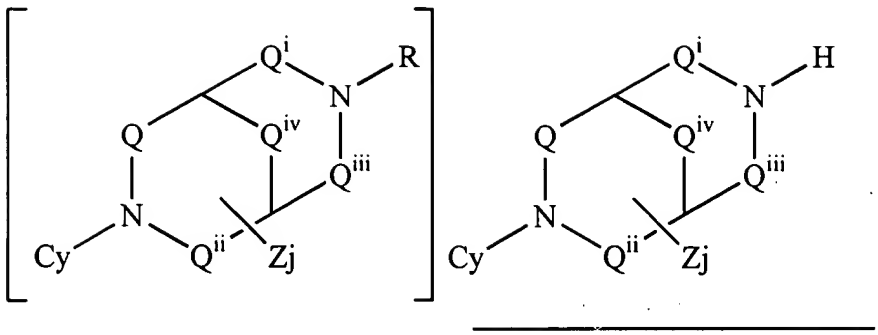
7. (Amended) The compound of Claim 6, wherein Y, Y', Y" and Y"' all are carbon bonded to a substituent species G.

8. (Amended) The compound of Claim 6, wherein one or two of Y, Y', Y" and Y"' are nitrogen and the remaining are carbon bonded to a substituent species G.

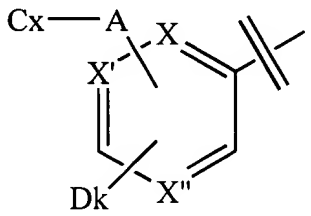
9. (Amended) The compound of Claim 6, wherein E', E and E' all are carbon bonded to substituent species G.

10. (Amended) The compound of Claim 6, wherein one or two of E', E" and E"' are nitrogen and the remaining are carbon bonded to substituent species G.

12. (Amended) A compound of the formula:



wherein Q is $(CH_2)_u$, Q^i is $(CH_2)_v$, Q^{ii} is $(CH_2)_w$, Q^{iii} is $(CH_2)_x$, and Q^{iv} is $(CH_2)_y$, where u, v, w and x are individually 0, 1, 2, 3 or 4 and y is 1 or 2; Z is a [non-hydrogen] substituent species [characterized as having a sigma m value between –0.3 and about 0.75] G; j is from 0 to 10; R is hydrogen or [lower] C_{1-8} alkyl; and Cy is



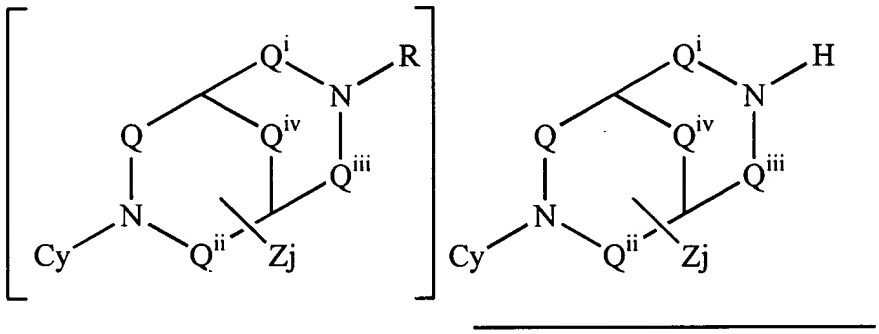
where each of X, X' and X" are individually nitrogen, nitrogen bonded to oxygen or carbon bonded to a substituent species [characterized as having a sigma m value between –0.3 and about 0.75] G; A is a covalent bond; D is a [non-hydrogen] substituent species [characterized as having a sigma m value between –0.3 and about 0.75] G; k is 0, 1 or 2; [and] Cx is selected from a group consisting of aryl, substituted aryl, heteroaryl, substituted heteroaryl, non-aromatic heterocyclyl, substituted non-aromatic heterocyclyl, non-aromatic heterocyclylalkyl and substituted non-aromatic heterocyclylalkyl, with the proviso that [the diazabicyclic ring is not 2,5-diazabicyclo[2.2.1]heptane and/or] Cx is not phenyl or substituted phenyl;

G is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, non-aromatic heterocyclyl, substituted non-aromatic heterocyclyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, alkylaryl, substituted alkylaryl, arylalkyl, substituted arylalkyl, -F, -Cl, -Br, -I, -OR', -NR'R -CF_3, -CN, -N_3, -NO_2, -C_2 R', -SR', -SOR', -SO_2 CH_3, -SO_2 NR'R -C(=O)NR'R", -NR'C(=O)R -NR'SO_2 R -C(=O)R', -C(=O)OR', -(CH_2)qOR', -OC(=O)R', -$(CR'R)_q$$OCH_2C_2$ R', -(CR'R)qC(=O)R', -O$(CR'R)_q$C(=O)R', -$C_2(CR'R')_q$OR', -$(CR'R)_q$NR'R -OC(=O)NR'R and -NR'C(=O)OR' where R' and R are individually hydrogen, C_{1-8} alkyl, an

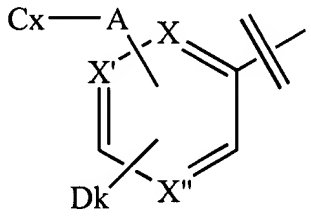
aromatic group-containing species or a substituted aromatic group-containing species, wherein the substituent is G and the aromatic group containing species is phenyl, biphenyl, naphthyl, pyridinyl, pyrimidinyl, quinolinyl, or indolyl,

and q is an integer from 1 to 6.

22. (Amended) A pharmaceutical composition useful for treatment of central nervous system disorders comprising a therapeutically effective amount of a compound of the formula:



wherein Q is $(CH_2)_u$, Q^i is $(CH_2)_v$, Q^{ii} is $(CH_2)_w$, Q^{iii} is $(CH_2)_x$, and Q^{iv} is $(CH_2)_y$, where u, v, w and x are individually 0, 1, 2, 3 or 4 and y is 1 or 2; wherein u, v, w and x are selected such that the ring is a diazabicyclononane; Z is a [non-hydrogen] substituent species [characterized as having a sigma m value between –0.3 and about 0.75] G; j is from 0 to 10; R is hydrogen or [lower] C_{1-8} alkyl; and Cy is



where each of X, X' and X" are individually nitrogen, nitrogen bonded to oxygen or carbon bonded to a substituent species [characterized as having a sigma m value between –0.3 and about 0.75] G; A is O or C=O; D is a [non-hydrogen] substituent species [characterized as

having a sigma m value between –0.3 and about 0.75] G; k is 0, 1 or 2; and Cx is selected from a group consisting of aryl, substituted aryl, heteroaryl, substituted heteroaryl, non-aromatic heterocyclyl, substituted non- aromatic heterocyclyl, non-aromatic heterocyclylalkyl and substituted non-aromatic heterocyclylalkyl,

wherein G is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, non-aromatic heterocyclyl, substituted non-aromatic heterocyclyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, alkylaryl, substituted alkylaryl, arylalkyl, substituted arylalkyl, -F, -Cl, -Br, -I, -OR', -NR'R -CF_3, -CN, -N_3, -NO_2, -C_2 R', -SR', -SOR', -SO_2 CH_3, -SO_2 NR'R -C(=O)NR'R", -NR'C(=O)R -NR'SO_2 R -C(=O)R', -C(=O)OR', -(CH_2)qOR', -OC(=O)R', -$(CR'R)_qOCH_2C_2$ R', -(CR'R)qC(=O)R', -$O(CR'R)_qC(=O)R'$, -$C_2(CR'R')_qOR'$, -$(CR'R)_qNR'R$ -OC(=O)NR'R and -NR'C(=O)OR' where R' and R are individually hydrogen, C_{1-8} alkyl, an aromatic group-containing species or a substituted aromatic group-containing species, wherein the substituent is G and the aromatic group containing species is phenyl, biphenyl, naphthyl, pyridinyl, pyrimidinyl, quinolinyl, or indolyl, and

q is an integer from 1 to 6.

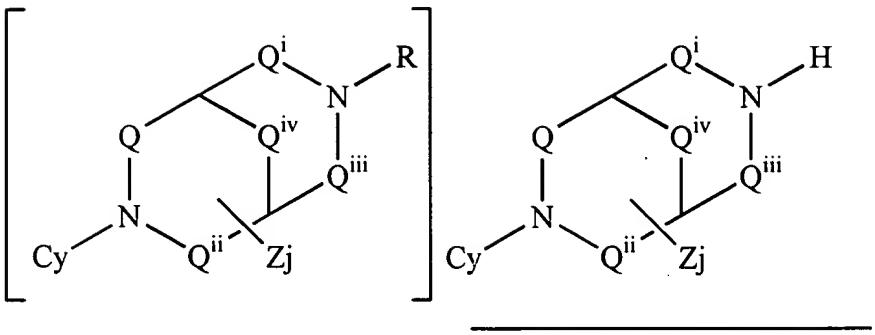
28. (Amended) The pharmaceutical composition of Claim 27, wherein Y, Y', Y" and Y"' all are carbon bonded to a substituent species G.

29. (Amended) The pharmaceutical composition of Claim 27, wherein one or two of Y, Y', Y" and Y"' are nitrogen and the remaining are carbon bonded to a substituent species G.

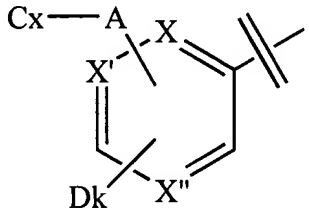
30. (Amended) The pharmaceutical composition of Claim 27, wherein E', E" and E"' all are carbon bonded to substituent species G.

31. (Amended) The pharmaceutical composition of Claim 27, wherein one or two of E', E" and E"' are nitrogen and the remaining are carbon bonded to substituent species G.

33. (Amended) A pharmaceutical composition useful for treatment of central nervous system disorders comprising a therapeutically effective amount of a compound of the formula:



wherein Q is $(CH_2)_u$, Q^i is $(CH_2)_v$, Q^{ii} is $(CH_2)_w$, Q^{iii} is $(CH_2)_x$, and Q^{iv} is $(CH_2)_y$, where u, v, w and x are individually 0, 1, 2, 3 or 4 and y is 1 or 2; Z is a [non-hydrogen] substituent species [characterized as having a sigma m value between –0.3 and about 0.75] G; j is from 0 to 10; R is hydrogen or [lower] C_{1-8} alkyl; and Cy is



where each of X, X' and X" are individually nitrogen, nitrogen bonded to oxygen or carbon bonded to a substituent species [characterized as having a sigma m value between –0.3 and about 0.75] G; A is a covalent bond; D is a [non-hydrogen] substituent species [characterized as having a sigma m value between –0.3 and about 0.75] G; k is 0, 1 or 2; [and] Cx is selected from a group consisting of aryl, substituted aryl, heteroaryl, substituted heteroaryl, non-aromatic heterocyclyl, substituted non-aromatic heterocyclyl, non-aromatic heterocyclylalkyl and substituted non-aromatic heterocyclylalkyl, with the proviso that [the diazabicyclic ring is not 2,5-diazabicyclo[2.2.1]heptane and/or] Cx is not phenyl or substituted phenyl;

G is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, non-aromatic heterocyclyl, substituted non-aromatic heterocyclyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, alkylaryl, substituted alkylaryl, arylalkyl, substituted arylalkyl, -F, -Cl, -Br, -I, -OR', -NR'R -CF_3, -CN, -N_3, -NO_2, -C_2 R', -SR', -SOR', -SO_2 CH_3, -SO_2 NR'R -C(=O)NR'R", -NR'C(=O)R -NR'SO_2 R -C(=O)R', -C(=O)OR', -(CH_2)qOR', -OC(=O)R', -$(CR'R)_q$$OCH_2C_2$ R', -(CR'R)qC(=O)R', -O$(CR'R)_q$C(=O)R', -$C_2(CR'R')_q$OR', -$(CR'R)_q$NR'R -

OC(=O)NR'R and -NR'C(=O)OR' where R' and R are individually hydrogen, C_{1-8} alkyl, an aromatic group-containing species or a substituted aromatic group-containing species, wherein the substituent is G and the aromatic group containing species is phenyl, biphenyl, naphthyl, pyridinyl, pyrimidinyl, quinolinyl, or indolyl,

and q is an integer from 1 to 6.

39. (Amended) The pharmaceutical composition of Claim 38, wherein Y, Y', Y" and Y"' all are carbon bonded to a substituent species G.

40. (Amended) The pharmaceutical composition of Claim 38, wherein one or two of Y, Y', Y" and Y"' are nitrogen and the remaining are carbon bonded to a substituent species G.

41. (Amended) The pharmaceutical composition of Claim 38, wherein E', E" and E"' all are carbon bonded to substituent species G.

42. (Amended) The pharmaceutical composition of Claim 38, wherein one or two of E', E" and E"' are nitrogen and the remaining are carbon bonded to substituent species G.